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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Friedman et al.

SERIAL NO.: CPA of 08/485,943

EXAMINER: Yucel R.

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FOR: MODULATORS OF BODY WEIGHT, CORRESPONDING NUCLEIC ACIDS AND PROTEINS, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF

#30
J. J.
5/15/00

CERTIFICATE OF MAILING UNDER 37 CFR §1.8

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Joan A. Santucci 5/8/00

(Signature and Date)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

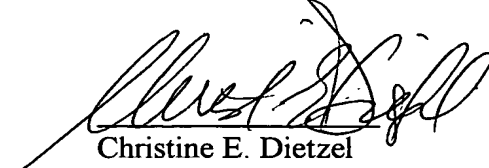
In accordance with Applicant's and Applicant's representatives' Duty of Disclosure under 37 CFR § 1.56, and pursuant to 37 CFR §1.97 and MPEP 717.05(b), Applicant(s) submit herewith documentary information for consideration by the Examiner. Information herein cited is only set forth in fulfillment of Applicant's duty of candor in disclosing all information brought to his attention, and is not an admission that it can be used adversely. The publications forwarded herewith are listed on the enclosed Form PTO-1449. Applicant(s) request that the Examiner, upon reviewing the enclosed materials, initial the enclosed form and return a copy thereof in accordance with the instructions on the form.

Enclosed please find copies of References **A41**, **A42** and **C119** listed on the attached Form PTO-1449. Reference **A41**, issued US Patent No. 5,512,457 of Lyman et al., is a priority document for Applicants' herein disclosed A35 reference. Reference **A42**, issued US Patent No. 5,098,833 of Lasky et al., is a priority document for Applicants' herein disclosed A36 reference. **C119** is the original Genbank entry of the Mus musculus obese (ob) mRNA, deposited by Zhang, Y. et al on December 21, 1994. This entry was replaced by the Genbank entry deposited on March 30, 1995, disclosed to the Examiner herein as reference **C30**.

In as much as a copy of References **A25** through **A40**, **B78** through **B90**, and **C1** through **C118** listed on the attached PTO Form 1449 have been earlier provided to the Examiner, particularly with regard to U.S. Application Serial No. 08/488,208 (Our Ref. 600-1-087CIP2B), they are not enclosed herewith. Should the Examiner wish a copy of any or all of these references, they will promptly be provided upon her request.

No fee is believed due for the filing of this statement inasmuch as it is being filed before the mailing of the first official action on the merits. However, should the Patent and Trademark Office determine otherwise, authorization is hereby given to charge Deposit Account No. 11-1153 for this filing.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Christine E. Dietzel", written over a horizontal line.

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#30 Attachment
08/485943

As a courtesy to the Examiner, and for ease of review, Applicants believe that the documents listed on the accompanying Form PTO-1449 may be organized as set forth below (each listing includes: Form PTO-1449 document number, title, inventor(s), patent number and/or application number, filing date, publication date, and where applicable, priority dates). As a further courtesy to the Examiner, the applicants have included, as Appendix A, a copy of the front page of each patent or patent application listed in the IDS and PTO Form-1449.



I. Proteins/Protein Analogs (Non-Leptin)

U.S. Patent Documents:

- A28 Title: "Cysteine Depleted IL-6 Muteins"
Inventors: Skelly et al.
U.S. Patent No.: 5,359,034
Issued: October 25, 1994
U.S. Appl. No.: 907,710
Filed: July 2, 1992
Priority Data: July 2, 1991 (U.S. Serial No. 724,698)
- A32 Title: "CD30 Ligand"
Inventors: Goodwin et al.
U.S. Patent No.: 5,480,981
Issued: January 2, 1996
U.S. Appl. No.: 225,989
Filed: April 12, 1994
Priority Data: October 27, 1992 (U.S. Serial No. 996,775)
July 1, 1992 (U.S. Serial No. 907,224)
June 15, 1992 (U.S. Serial No. 899,660)
June 2, 1992 (U.S. Serial No. 892,459)
May 26, 1992 (U.S. Serial No. 889,717)
- A41 Title: "Cytokine Designated Elk Ligand"
Inventors: Lyman et al.
U.S. Patent No.: 5,512,457
Issued: April 30, 1996
U.S. Appl. No.: 213,403
Filed: March 15, 1994
Priority Data: November 13, 1992 (U.S. Serial No. 977,693)

A42 Title: "DNA Sequence Encoding a Functional Domain of a Lymphocyte Homing Receptor"
Inventors: Lasky et al.
U.S. Patent No.: 5,098,833
Issued: March 24, 1992
U.S. Appl. No.: 315,015
Filed: February 23, 1989

Foreign Patent Documents:

B80 Title: "The Manufacture and Expression of Large Structural Genes"
Inventors: Alton et al.
Appl. No.: PCT/US83/00605
Filed: April 25, 1983
Publication No.: WO 83/04053
Publication Date: November 24, 1983
Priority Data: May 6, 1982 (U.S. Appl. No. 375,494)
April 15, 1983 (U.S. Appl. No. 483,451)

B81 Title: "Compositions and Method for Treating or Preventing Infections in Animals"
Inventors: Boone et al.
Appl. No.: PCT/US89/02057
Filed: May 12, 1989
Publication No.: WO 89/10932
Publication Date: November 16, 1989
Priority Data: May 13, 1988 (U.S. Appl. No. 193,857)
May 9, 1989 (U.S. Appl. No. 348,011)

Non-Patent Documents:

- C57 Kaiser, E.T. *et al.*, "Amphiphilic Secondary Structure: Design of Peptide Hormones," *Science*, 223:249-255 (January, 1984).
- C67 Lerner, R.A., "Synthetic Vaccines," *Scientific American*, 248:66-74 (1983).

II. Fusion Proteins

U.S. Patent Documents:

- A25 Title: "Fusion Proteins Comprising GM-CSF and IL-3"
Inventors: Curtis et al.
U.S. Patent No.: 5,073,627
Issued: December 17, 1991
U.S. Appl. No.: 567,983
Filed: August 14, 1990
Priority Data: August 22, 1989 (U.S. Serial No. 397,146)
- A26 Title: "Hybrid Immunoglobulins"
Inventors: Capon et al.
U.S. Patent No.: 5,116,964
Issued: May 26, 1992
U.S. Appl. No.: 440,625
Filed: November 22, 1989
Priority Data: February 23, 1989 (U.S. Serial No. 315,015)
- A27 Title: "Lymphocyte Homing Receptor/Immunoglobulin Fusion Proteins"
Inventors: Capon et al.
U.S. Patent No.: 5,225,538
Issued: July 6, 1993
U.S. Appl. No.: 808,122
Filed: December 16, 1991
Priority Data: November 22, 1989 (U.S. Serial No. 440,625;
U.S. Patent No. 5,116,964; Issued May 26, 1992)
February 23, 1989 (U.S. Serial No. 315,015; U.S.
Patent No. 5,098,833; Issued March 24, 1992)

- A29 Title: "Hybrid Immunoglobulins"
Inventors: Capon et al.
U.S. Patent No.: 5,428,130
Issued: June 27, 1995
U.S. Appl. No.: 986,931
Filed: December 8, 1992
Priority Data: December 16, 1991 (U.S. Serial No. 808,122;
U.S. Patent No. 5,225,538; Issued July 6, 1993)
November 22, 1989 (U.S. Serial No. 440,625;
U.S. Patent No. 5,116,964; Issued May 26, 1992)
February 23, 1989 (U.S. Serial No. 315,015; U.S.
Patent No. 5,098,833; Issued March 24, 1992)
- A30 Title: "DNA Encoding a Chimeric Polypeptide Comprising the
Extracellular Domain of TNF Receptor Fused to IgG, Vectors,
and Host Cells"
Inventors: Beutler et al.
U.S. Patent No.: 5,447,851
Issued: September 5, 1995
U.S. Appl. No.: 862,495
Filed: April 2, 1992
- A31 Title: "Expression Vector Encoding Hybrid Immunoglobulins"
Inventors: Capon et al.
U.S. Patent No.: 5,455,165
Issued: October 3, 1995
U.S. Appl. No.: 185,669
Filed: January 21, 1994
Priority Data: December 8, 1992 (U.S. Serial No. 986,931)
December 16, 1991 (U.S. Serial No. 808,122;
U.S. Patent No. 5,225,538; Issued July 6, 1993)
November 22, 1989 (U.S. Serial No. 440,625;
U.S. Patent No. 5,116,964; Issued May 26, 1992)
February 23, 1989 (U.S. Serial No. 315,015; U.S.
Patent No. 5,098,833; Issued March 24, 1992)

- A33 Title: "Recombinant DNA Encoding Hybrid Immunoglobulins"
Inventors: Capon et al.
U.S. Patent No.: 5,514,582
Issued: May 7, 1996
U.S. Appl. No.: 185,670
Filed: January 21, 1994
Priority Data: December 8, 1992 (U.S. Serial No. 986,931; U.S. Patent No. 5,428,130; Issued June 27, 1995)
December 16, 1991 (U.S. Serial No. 808,122; U.S. Patent No. 5,225,538; Issued July 6, 1993)
November 22, 1989 (U.S. Serial No. 440,625; U.S. Patent No. 5,116,964; Issued May 26, 1992)
February 23, 1989 (U.S. Serial No. 315,015; U.S. Patent No. 5,098,833; Issued March 24, 1992)
- A35 Title: "Elk Ligand Fusion Proteins"
Inventors: Lyman et al.
U.S. Patent No.: 5,670,625
Issued: September 23, 1997
U.S. Appl. No.: 460,741
Filed: June 2, 1995
Priority Data: March 15, 1994 (U.S. Serial No. 213,403; U.S. Patent No. 5,512,457; Issued April 30, 1996)
November 13, 1992 (U.S. Serial No. 977,693)
- A36 Title: "Hybrid Immunoglobulins"
Inventors: Capon et al.
U.S. Patent No.: 5,714,147
Issued: February 3, 1998
U.S. Appl. No.: 451,848
Filed: May 26, 1995
Priority Data: January 21, 1994 (U.S. Serial No. 185,670; U.S. Patent No. 5,514,582; Issued May 7, 1996)
December 8, 1992 (U.S. Serial No. 986,931; U.S. Patent No. 5,428,130; Issued June 27, 1995)
December 19, 1991 (U.S. Serial No. 808,122; U.S. Patent No. 5,225,538; Issued July 6, 1993)
November 22, 1989 (U.S. Serial No. 440,625; U.S. Patent No. 5,116,964; Issued May 26, 1992)
February 23, 1989 (U.S. Serial No. 315,015; U.S. Patent No. 5,098,833; Issued March 24, 1992)

A38 Title: "Altered Polypeptides with Increased Half-life"
Inventors: Presta et al.
U.S. Patent No.: 5,739,277
Issued: April 14, 1998
U.S. Appl. No.: 422,101
Filed: April 14, 1995

Foreign Patent Documents:

- B84 Title: "Pharmaceutical Compositions Comprising a Chimeric TNF Binding Protein"
Inventors: Booth et al.
Appl. No.: PCT/EP95/02788
Filed: July 15, 1995
Publication No.: WO 96/03141
Publication Date: February 8, 1996
Priority Data: July 22, 1994 (EP Appl. No. 94111455.5)
- B85 Title: "Novel Compounds"
Inventors: Browne et al.
Appl. No.: PCT/EP95/03036
Filed: July 28, 1995
Publication No.: WO 96/04388
Publication Date: February 15, 1996
Priority Data: July 29, 1994 (G.B. Appl. No. 9415379.8)
June 6, 1995 (U.S. Appl. No. 08/468,297)
- B88 Title: "Chimeric Cytokines and Uses Thereof"
Inventors: Strom et al.
Appl. No.: PCT/US95/16046
Filed: December 12, 1995
Publication No.: WO 96/18412
Publication Date: June 20, 1996
Priority Data: December 12, 1994 (U.S. Appl. No. 08/355,502)
April 28, 1995 (U.S. Appl. No. 08/431,535)

B90 Title: "Hybrid with Interferon - α and an Immunoglobulin Fc Linked Through a Non-Immunogenic Peptide"
 Inventors: Chang et al.
 Appl. No.: PCT/US96/20861
 Filed: December 13, 1996
 Publication No.: WO 97/24137
 Publication Date: July 10, 1997
 Priority Data: December 28, 1995 (U.S. Appl. No. 08/579,211)
 September 25, 1996 (U.S. Appl. No. 08/719,331)

Non-Patent Documents:

- C9 Capon, D.J. *et al.*, "Designing CD4 immunoadhesins for AIDS therapy," *Nature*, 337:525-531 (February, 1989).
- C18 Ellison, J.W. *et al.*, "The nucleotide sequence of a human immunoglobulin C γ_1 gene," *Nucleic Acids Research*, 10(13):4071-4079 (1982).
- C22 Fisher, C.J. *et al.*, "Treatment of Septic Shock with the Tumor Necrosis Factor Receptor:Fc Fusion Protein," *N. Engl. J. Med.*, 334:1697-1702 (1996).
- C24 Ford, C.F. *et al.*, "Fusion Tails for the Recovery and Purification of Recombinant Proteins," *Protein Expression and Purification*, 2:95-107 (1991).
- C36 Harvill, E.T. *et al.*, "An IgG3-IL2 fusion protein activates complement, binds Fc γ RI, generates LAK activity and shows enhanced binding to the high affinity IL-2R," *Immunotechnology*, 1:95-105 (1995).
- C47 Huse, W.D. *et al.*, "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," *Science*, 246:1275-1281 (December, 1989).
- C48 IBI FLAG BIOSYSTEM, "High Yield Expression, Detection, and Purification of Recombinant Proteins in E. coli," Integrated Sciences Pty Ltd, Sydney, Australia
- C49 IBI FLAG Epitope, A Technical Bulletin for Users of FLAG Technology, International Biotechnologies Inc., FLAG Product Development Group, IBI, A Kodak Company, New Haven, CT, Volume 1, Number 1, pp. 1-24 (September, 1992).

- C76 Mini-Symposium on Flag Technology, ASCB 1992, "Purification and Characterization of Cellular Proteins with the Flag Epitope," Colorado Convention Center, Denver, Colorado, 8 pages (November 18, 1992)
- C84 Palmiter, R.D. *et al.*, "Metallothionein-Human GH Fusion Genes Stimulate Growth of Mice," *Science*, 222:809-814 (November, 1983).
- C103 Van Zee, K. *et al.*, "Protection Against Lethal Escherichia coli Bacteremia in Baboons (*Papio anubis*) by Pretreatment with a 55-kDa TNF Receptor (CD120a)-Ig Fusion Protein, Ro 45-2081¹," *The Journal of Immunology*, 156:2221-2230 (1996).
- C117 Zheng, X. *et al.*, "Administration of Noncytolytic IL-10/Fc in Murine Models of Lipopolysaccharide-Induced Septic Shock and Allogeneic Islet Transplantation," *The Journal of Immunology*, 154:5590-5600 (1995).

III. Protein Derivatives/Conjugates

U.S. Patent Documents:

- A34 Title: "Conjugates of Vitamin B12 and Proteins"
 Inventors: Habberfield et al.
 U.S. Patent No.: 5,574,018
 Issued: November 12, 1996
 U.S. Appl. No.: 282,384
 Filed: July 29, 1994

Foreign Patent Documents:

- B79 Title: "Chemically Modified Granulocyte Colony Stimulating Factor"
 Inventors: Ishikawa et al.
 Appl. No.: 90900360.0
 Filed: December 22, 1989
 Publication No.: EP 0 401 384
 Publication Date: December 12, 1990
 Priority Data: December 22, 1988 (JP Appl. No. 324747/88)
 July 31, 1989 (JP Appl. No. 199176/89)

- B82 Title: "Pulmonary Administration of Granulocyte Colony Stimulating Factor"
Inventors: Niven et al.
Appl. No.: PCT/US94/01875
Filed: February 22, 1994
Publication No.: WO 94/20069
Publication Date: September 15, 1994
Priority Data: March 8, 1993 (U.S. Appl. No. 08/028,087)
- B83 Title: "Oral Delivery of Chemically Modified Proteins"
Inventors: Habberfield, A.
Appl. No.: PCT/US95/01752
Filed: February 8, 1995
Publication No.: WO 95/21629
Publication Date: August 17, 1995
Priority Data: February 8, 1994 (U.S. Appl. No. 08/194,187)
February 1, 1995 (U.S. Appl. No. 08/379,121)
- B87 Title: "N-terminally Chemically Modified Protein Compositions and Methods"
Inventors: Kinstler et al.
Appl. No.: PCT/US95/01729
Filed: February 8, 1995
Publication No.: WO 96/11953
Publication Date: April 25, 1996
Priority Data: October 12, 1994 (U.S. Appl. No. 08/321,510)
- B89 Title: "Stable Protein: Phospholipid Compositions and Methods"
Inventors: Collins et al.
Appl. No.: PCT/US96/04261
Filed: March 28, 1996
Publication No.: WO 96/29989
Publication Date: October 3, 1996
Priority Data: March 31, 1995 (U.S. Appl. No. 08/414,161)

IV. Antibodies

Non-Patent Documents:

- C4 Baron, M.H. *et al.*, "Antibodies against the Chemically Synthesized Genome-Linked Protein of Poliovirus React with Native Virus-Specific Proteins," *Cell*, 28:395-404 (February, 1982).

- C17 Dressman, G.R. *et al.*, "Antibody to hepatitis B surface antigen after a single inoculation of uncoupled synthetic HbsAg peptides," *Nature*, 295:158-160 (January, 1982).
- C64 Köhler, G. *et al.*, "Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion," *Eur. J. Immunol.*, 6:511-519 (1976).
- C65 Lerner, R.A. *et al.*, "Antibodies to Chemically Synthesized Peptides Predicted from DNA Sequences as Probes of Gene Expression," *Cell*, 23:309-310 (February, 1981).
- C66 Lerner, R.A. *et al.*, "Chemically synthesized peptides predicted from the nucleotide sequence of the hepatitis B virus genome elicit antibodies reactive with the native envelope protein of Dane particles," *Proc. Natl. Acad. Sci., USA*, 78(6):3403-3407 (June, 1981).

V. Leptin Proteins/Analog

U.S. Patent Documents:

- A37 Title: "Anti-Obesity Proteins"
 Inventors: DiMarchi et al.
 U.S. Patent No.: 5,719,266
 Issued: February 17, 1998
 U.S. Appl. No.: 406,354
 Filed: March 17, 1995

Foreign Patent Documents:

- B78 Title: "Recombinant Obese (OB) Proteins"
 Inventors: Campfield et al.
 Appl. No.: 51978/96
 Filed: April 30, 1996
 Publication No.: AU-B-51978/96
 Publication Date: March 5, 1998
 Priority Data: May 5, 1995 (U.S. Appl. No. 435,777)
 June 7, 1995 (U.S. Appl. No. 484,629)

B86 Title: "Modulators of Body Weight, Corresponding Nucleic Acids and Diagnostic and Therapeutic Uses Thereof"
 Inventors: Friedman et al.
 Appl. No.: PCT/US95/10479
 Filed: August 17, 1995
 Publication No.: WO 96/05309
 Publication Date: February 22, 1996
 Priority Data: August 17, 1994 (U.S. Appl. No. 08/292,345)
 November 30, 1994 (U.S. Appl. No. 08/347,563)
 May 10, 1995 (U.S. Appl. No. 08/438,431)
 June 7, 1995 (U.S. Appl. No. 08/483,211)

Non-Patent Documents:

- C1 Altman, S.W. *et al.*, "Expression and Purification of a Synthetic Human Obese Gene Product," *Protein Expression and Purification*, 6:722-726 (1995).
- C27 GenBank Accession No. 603288, ob, Deposited by Zhang et al., March 30, 1995.
- C28 GenBank Accession No. 623332, ob, Deposited by Zhang *et al.*, January 13, 1995.
- C29 GenBank Accession No. 726297, obesity protein, Deposited by Chehab *et al.*, March 21, 1995.
- C30 GenBank Accession No. U18812, Mus musculus obese precursor (ob) mRNA, complete cds., deposited by Zhang, Y. et al., March 30, 1995. [This sequence version replaced gi:603287, submitted December 21, 1994, disclosed below as reference C119, which contained an inadvertent error in upstream non-coding sequence.]
- C31 GenBank Accession No. U18915, Human obese (ob) mRNA, complete cds., deposited by Zhang, Y. et al., January 13, 1995.
- C32 GenBank Accession No. U22421, Mus musculus obesity protein (ob) gene, complete cds., Deposited by Chehab *et al.*, March 23, 1995.
- C119 GenBank Accession No. U18812, Mus musculus obese precursor (ob) mRNA, complete cds., deposited by Zhang, Y. et al., December 21, 1994. [This entry was replaced by the GenBank entry deposited on March 30, 1995, disclosed above as reference C30.]

VI. OB Gene/Gene Expression

Non-Patent Documents:

- C12 Coleman, D.L. et al., "The Influence of Genetic Background on the Expression of the Obese (*Ob*) Gene in the Mouse," *Diabetologia*, 9:287-293 (1973).
- C14 Considine, R.V. et al., "Ob Gene Expression Is Increased in Adipocytes from Obese Humans," *Diabetes*, 44:202A (May, 1995) (ABSTRACT 739).
- C25 Frederich, R. et al., "Nutritional Regulation of ob Gene mRNA in White Adipose Tissue," The Endocrine Society, Programs & Abstracts, 77th Meeting, June 14-17, 1995, Washington, D.C., p.173 (ABSTRACT OR25-3)
- C35 Hamilton, B.S. et al., "Increased obese mRNA expression in omental fat cells from massively obese humans," *Nature Medicine*, 1(9):953-956 (September, 1995).
- C38 He, Y. et al., "The Mouse *obese* Gene," *Journal of Biological Chemistry*, 270(48):28887-28891 (December, 1995).
- C52 Isse N. et al., "Structural Organization and Chromosomal Assignment of the Human obese Gene," *J. Biological Chemistry*, 270(46):27728-27733 (November, 1995).
- C73 Masuzaki et al., "Molecular Cloning of a Rat Obese (*ob*) Complement DNA - Augmented Gene Expression in Obese-Hyperglycemic Wistar Fatty Rats," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.175 (ABSTRACT P1-250)
- C74 Masuzaki, H. et al., "Adipose Tissue-specific Expression of the *Obese* (*ob*) Gene in Rats and Its Marked Augmentation in Genetically Obese-hyperglycemic Wistar Fatty Rats," *Proceedings of the Japan Academy Series B Physical and Biological Sciences*, 71(5):148-152 (1995).
- C77 Mizuno, T. et al., "Elevated Expression of Obese (*ob/ob*) Gene Product in Adipose Tissue, and Impaired Induction by Insulin of Jun-B mRNA in Liver, in Genetically Obese Yellow Mice," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.174 (ABSTRACT P1-248)
- C78 Moinat, M. et al., "Modulation of *obese* gene expression in rat brown and white adipose tissues," *FEBS Letters*, 373:131-134

(1995).

- C80 Murakami, T. *et al.*, "Cloning of Rat *Obese* cDNA and its Expression in Obese Rats," *Biochemical and Biophysical Research Communications*, 209(3):944-952 (April, 1995).
- C81 Nakamura, M.T. , "Another Obese Gene Function," *Nature*, 374:124 (March, 1995).
- C82 Ogawa, *et al.*, "Region-Specificities of the Obese (ob) Gene Expression in Adipose Tissue in Mice and Altered Gene Expression in C57BL/6J ob/ob Mice," *The Endocrine Society, Programs and Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C.*, p.175 (ABSTRACT P1-249).
- C89 Reddy, R. *et al.*, "Equivalent Levels of OB Gene Expression in Adipose Tissues of Morbidly Obese and Lean Patients," *The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C.*, (ABSTRACT P3-266).
- C93 Shigemoto, M. *et al.*, "Tissue Distribution of the Obese (ob) Gene Expression in Mice and Augmented Gene Expression in the ob/ob Mice," *Diabetes*, 44:204A (May, 1995) (ABSTRACT 748).
- C96 Stirling B. *et al.*, "Identification of Microsatellite Markers Near the Human ob Gene and Linkage Studies in NIDDM-Affected Sib Pairs," *Diabetes*, 44: 999-1001 (August, 1995).
- C104 Vydelingum S. *et al.*, " Overexpression of the Obese Gene in the Genetically Obese JCR:LA-Corpulent Rat," *Biochemical and Biophysical Research Communications*, 216(1):148-153 (November, 1995).
- C116 Zhang, B. *et al.*, "Down-regulation of the Expression of the *Obese* Gene by an Antidiabetic Thiazolidinedione in Zucker Diabetic Fatty Rats and *db/db* Mice," *J. Biological Chemistry*, 271(16):9455-9459 (April, 1996).

VII. Leptin/Methods of Treatment

U.S. Patent Documents:

- A39 Title: "Methods for Treating Diabetes"
Inventors: Stephens
U.S. Patent No.: 5,756,461
Issued: May 26, 1998
U.S. Appl. No.: 678,369
Filed: June 28, 1996
Priority Data: June 30, 1995 (U.S. Serial No. 60/000,718)
- A40 Title: "Materials and Methods for Determining Ob Protein in a Biological Sample"
Inventors: Weigle et al.
U.S. Patent No.: 5,827,734
Issued: October 27, 1998
U.S. Appl. No.: 540,242
Filed: October 27, 1998
Priority Data: June 7, 1995 (U.S. Serial No. 486,459)
June 7, 1995 (U.S. Serial No. 486,450)
June 7, 1995 (U.S. Serial No. 487,111)
April 10, 1995 (U.S. Serial No. 419,214)
January 20, 1995 (U.S. Serial No. 377,068)

Non-Patent Documents:

- C2 Angier, N., "Researchers Link Obesity In Humans To Flaw In A Gene," *The New York Times* reported on December 1, 1994.
- C3 Barinaga, " 'Obese' Protein Slims Mice", *Science*, 269:475-476 (July, 1995).
- C6 Bishop, J.E., "Newfound Gene May Control Fat Storage," *The Wall Street Journal, Health and Science*, reported on December 1, 1994.
- C7 Bishop, J.E., "Rockefeller Study Supports Theory That Body Has Fat-Maintenance System," *Wall Street Journal*, reported on March 9, 1995.
- C15 Cusin I. *et al.*, "The *ob* Gene and Insulin A Relationship Leading to Clues to the Understanding of Obesity," *Diabetes*, 44:1467-1470 (December, 1995).

- C16 Detjen, J. (Philadelphia Inquirer), "Obesity gene find may help millions someday," *The Durham Herald Co., The Herald-Sun* (Durham, NC), pg. A1, reported on December 1, 1994.
- C21 Ferré, P, "Obésité. Produit de Gène ob Et Contrôle De La Masse Adipeuse [Obesity, The ob Gene Product and Control of Adipose Mass]," *Diabete & Metabolisme (Paris)*, 21:217-218 (1995).
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